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(51) International Patent Classification ⁷ : A61K 38/17, 39/395, G01N 33/53, C12N 15/11, C07K 16/18, C12Q 1/68, G01N 33/68, A61K 48/00, C12N 15/867, 15/12, 1/21, 1/19, 5/10, C07K 14/47, 19/00		A2	(11) International Publication Number: WO 00/32221 (43) International Publication Date: 8 June 2000 (08.06.00)																																																						
(21) International Application Number: PCT/US99/28313 (22) International Filing Date: 30 November 1999 (30.11.99) (30) Priority Data: <table border="0"> <tr><td>PCT/US98/25108</td><td>1 December 1998 (01.12.98)</td><td>US</td></tr> <tr><td>60/112,850</td><td>16 December 1998 (16.12.98)</td><td>US</td></tr> <tr><td>60/115,554</td><td>12 January 1999 (12.01.99)</td><td>US</td></tr> <tr><td>PCT/US99/05028</td><td>8 March 1999 (08.03.99)</td><td>US</td></tr> <tr><td>60/123,957</td><td>12 March 1999 (12.03.99)</td><td>US</td></tr> <tr><td>60/131,445</td><td>28 April 1999 (28.04.99)</td><td>US</td></tr> <tr><td>60/134,287</td><td>14 May 1999 (14.05.99)</td><td>US</td></tr> <tr><td>PCT/US99/12252</td><td>2 June 1999 (02.06.99)</td><td>US</td></tr> <tr><td>60/141,037</td><td>23 June 1999 (23.06.99)</td><td>US</td></tr> <tr><td>60/144,758</td><td>20 July 1999 (20.07.99)</td><td>US</td></tr> <tr><td>60/145,698</td><td>26 July 1999 (26.07.99)</td><td>US</td></tr> <tr><td>PCT/US99/20111</td><td>1 September 1999 (01.09.99)</td><td>US</td></tr> <tr><td>PCT/US99/20594</td><td>8 September 1999 (08.09.99)</td><td>US</td></tr> <tr><td>PCT/US99/20944</td><td>13 September 1999 (13.09.99)</td><td>US</td></tr> <tr><td>PCT/US99/21090</td><td>15 September 1999 (15.09.99)</td><td>US</td></tr> <tr><td>PCT/US99/21547</td><td>15 September 1999 (15.09.99)</td><td>US</td></tr> <tr><td>PCT/US99/23089</td><td>5 October 1999 (05.10.99)</td><td>US</td></tr> <tr><td>60/162,506</td><td>29 October 1999 (29.10.99)</td><td>US</td></tr> </table>		PCT/US98/25108	1 December 1998 (01.12.98)	US	60/112,850	16 December 1998 (16.12.98)	US	60/115,554	12 January 1999 (12.01.99)	US	PCT/US99/05028	8 March 1999 (08.03.99)	US	60/123,957	12 March 1999 (12.03.99)	US	60/131,445	28 April 1999 (28.04.99)	US	60/134,287	14 May 1999 (14.05.99)	US	PCT/US99/12252	2 June 1999 (02.06.99)	US	60/141,037	23 June 1999 (23.06.99)	US	60/144,758	20 July 1999 (20.07.99)	US	60/145,698	26 July 1999 (26.07.99)	US	PCT/US99/20111	1 September 1999 (01.09.99)	US	PCT/US99/20594	8 September 1999 (08.09.99)	US	PCT/US99/20944	13 September 1999 (13.09.99)	US	PCT/US99/21090	15 September 1999 (15.09.99)	US	PCT/US99/21547	15 September 1999 (15.09.99)	US	PCT/US99/23089	5 October 1999 (05.10.99)	US	60/162,506	29 October 1999 (29.10.99)	US	(71) Applicant (for all designated States except US): GENENTECH, INC. [US/US]; 1 DNA Way, South San Francisco, CA 94080-4990 (US). (72) Inventors; and (75) Inventors/Applicants (for US only): ASHKENAZI, Avi, J. [US/US]; 1456 Tarrytown Street, San Mateo, CA 94402 (US). BAKER, Kevin, P. [GB/US]; 14006 Indian Run Drive, Darnestown, MD 20878 (US). FERRARA, Napoleone [US/US]; 2090 Pacific Avenue, #704, San Francisco, CA 94109 (US). GERBER, Hanspeter [CH/US]; 1121 Tennessee Street, #5, San Francisco, CA 94107 (US). HILLAN, Kenneth, J. [GB/US]; 64 Seward Street, San Francisco, CA 94114 (US). GODDARD, Audrey [CA/US]; 110 Congo Street, San Francisco, CA 94131 (US). GODOWSKI, Paul, J. [US/US]; 2627 Easton Drive, Burlingame, CA 94010 (US). GURNEY, Austin, L. [US/US]; 1 Debbie Lane, Belmont, CA 94002 (US). KLEIN, Robert, D. [US/US]; 1044 Webster Street, Palo Alto, CA 94301 (US). KUO, Sophia, S. [US/US]; 59 Surrey Street #3, San Francisco, CA 94131 (US). PAONI, Nicholas, F. [US/US]; 1756 Terrace Drive, Belmont, CA 94002 (US). SMITH, Victoria [AU/US]; 19 Dwight Road, Burlingame, CA 94010 (US). WATANABE, Colin, K. [US/US]; 128 Corliss Drive, Moraga, CA 94556 (US). WILLIAMS, P., Mickey [US/US]; 509 Alto Avenue, Half Moon Bay, CA 94019 (US). WOOD, William, I. [US/US]; 35 Southdown Court, Hillsborough, CA 94010 (US). (74) Agents: BARNES, Elizabeth, M. et al.; Genentech, Inc., 1 DNA Way, South San Francisco, CA 94080-4990 (US). (81) Designated States: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, ARIPO patent (GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG). Published Without international search report and to be republished upon receipt of that report.	
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(54) Title: PROMOTION OR INHIBITION OF ANGIOGENESIS AND CARDIOVASCULARIZATION																																																									
(57) Abstract <p>Compositions and methods are disclosed for stimulating or inhibiting angiogenesis and/or cardiovascularization in mammals, including humans. Pharmaceutical compositions are based on polypeptides or antagonists thereto that have been identified for one or more of these uses. Disorders that can be diagnosed, prevented, or treated by the compositions herein include trauma such as wounds, various cancers, and disorders of the vessels including atherosclerosis and cardiac hypertrophy. In addition, the present invention is directed to novel polypeptides and to nucleic acid molecules encoding those polypeptides. Also provided herein are vectors and host cells comprising those nucleic acid sequences, chimeric polypeptide molecules comprising the polypeptides of the present invention fused to heterologous polypeptide sequences, antibodies which bind to the polypeptides of the present invention and to methods for producing the polypeptides of the present invention.</p>																																																									

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WHAT IS CLAIMED IS:

1. A composition comprising a PRO172, PRO178, PRO179, PRO182, PRO187, PRO188, PRO195, PRO212, PRO214, PRO217, PRO224, PRO231, PRO235, PRO245, PRO261, PRO269, PRO287, PRO301, PRO323, PRO331, PRO356, PRO364, PRO526, PRO538, PRO713, PRO719, PRO771, PRO788, PRO792, PRO812, PRO865, PRO1075, PRO1126, PRO1130, PRO1154, PRO1244, PRO1246, PRO1274, PRO1286, PRO1294, PRO1303, PRO1304, PRO1312, PRO1313, PRO1376, PRO1387, PRO1561 or PRO216 polypeptide or agonist or antagonist thereof, in admixture with a pharmaceutically acceptable carrier.

2. The composition of Claim 1 comprising a therapeutically effective amount of said polypeptide or said agonist or antagonist thereof.

3. The composition of Claim 1, wherein the agonist is an anti-PRO172, anti-PRO178, anti-PRO179, anti-PRO182, anti-PRO187, anti-PRO188, anti-PRO195, anti-PRO212, anti-PRO214, anti-PRO217, anti-PRO224, anti-PRO231, anti-PRO235, anti-PRO245, anti-PRO261, anti-PRO269, anti-PRO287, anti-PRO301, anti-PRO323, anti-PRO331, anti-PRO356, anti-PRO364, anti-PRO526, anti-PRO538, anti-PRO713, anti-PRO719, anti-PRO771, anti-PRO788, anti-PRO792, anti-PRO812, anti-PRO865, anti-PRO1075, anti-PRO1126, anti-PRO1130, anti-PRO1154, anti-PRO1244, anti-PRO1246, anti-PRO1274, anti-PRO1286, anti-PRO1294, anti-PRO1303, anti-PRO1304, anti-PRO1312, anti-PRO1313, anti-PRO1376, anti-PRO1387, anti-PRO1561 or anti-PRO216 antibody.

4. The composition of Claim 1, wherein the antagonist is an anti-PRO172, anti-PRO178, anti-PRO179, anti-PRO182, anti-PRO187, anti-PRO188, anti-PRO195, anti-PRO212, anti-PRO214, anti-PRO217, anti-PRO224, anti-PRO231, anti-PRO235, anti-PRO245, anti-PRO261, anti-PRO269, anti-PRO287, anti-PRO301, anti-PRO323, anti-PRO331, anti-PRO356, anti-PRO364, anti-PRO526, anti-PRO538, anti-PRO713, anti-PRO719, anti-PRO771, anti-PRO788, anti-PRO792, anti-PRO812, anti-PRO865, anti-PRO1075, anti-PRO1126, anti-PRO1130, anti-PRO1154, anti-PRO1244, anti-PRO1246, anti-PRO1274, anti-PRO1286, anti-PRO1294, anti-PRO1303, anti-PRO1304, anti-PRO1312, anti-PRO1313, anti-PRO1376, anti-PRO1387, anti-PRO1561 or anti-PRO216 antibody.

5. The composition of Claim 1 further comprising a cardiovascular, endothelial, angiogenic or angiostatic agent.

6. A method of preparing the composition of Claim 1 comprising admixing a PRO172, PRO178, PRO179, PRO182, PRO187, PRO188, PRO195, PRO212, PRO214, PRO217, PRO224, PRO231, PRO235, PRO245, PRO261, PRO269, PRO287, PRO301, PRO323, PRO331, PRO356, PRO364, PRO526, PRO538, PRO713, PRO719, PRO771, PRO788, PRO792, PRO812, PRO865, PRO1075, PRO1126, PRO1130, PRO1154, PRO1244, PRO1246, PRO1274, PRO1286, PRO1294, PRO1303, PRO1304, PRO1312, PRO1313, PRO1376, PRO1387, PRO1561 or PRO216 polypeptide or agonist or antagonist thereof, with a pharmaceutically acceptable carrier.

7. An article of manufacture comprising:

- (1) composition comprising (a) a PRO172, PRO178, PRO179, PRO182, PRO187, PRO188, PRO195, PRO212, PRO214, PRO217, PRO224, PRO231, PRO235, PRO245, PRO261, PRO269, PRO287, PRO301, PRO323, PRO331, PRO356, PRO364, PRO526, PRO538, PRO713, PRO719, PRO771, PRO788, PRO792, PRO812, PRO865, PRO1075, PRO1126, PRO1130, PRO1154, PRO1244, PRO1246, PRO1274, PRO1286, PRO1294, PRO1303, PRO1304, PRO1312, PRO1313, PRO1376, PRO1387, PRO1561 or PRO216 polypeptide, (b) an agonist of a PRO172, PRO178, PRO179, PRO182, PRO187, PRO188, PRO195, PRO212, PRO214, PRO217, PRO224, PRO231, PRO235, PRO245, PRO261, PRO269, PRO287, PRO301, PRO323, PRO331, PRO356, PRO364, PRO526, PRO538, PRO713, PRO719, PRO771, PRO788, PRO792, PRO812, PRO865, PRO1075, PRO1126, PRO1130, PRO1154, PRO1244, PRO1246, PRO1274, PRO1286, PRO1294, PRO1303, PRO1304, PRO1312, PRO1313, PRO1376, PRO1387, PRO1561 or PRO216 polypeptide, or (c) an antagonist of a PRO172, PRO178, PRO179, PRO182, PRO187, PRO188, PRO195, PRO212, PRO214, PRO217, PRO224, PRO231, PRO235, PRO245, PRO261, PRO269, PRO287, PRO301, PRO323, PRO331, PRO356, PRO364, PRO526, PRO538, PRO713, PRO719, PRO771, PRO788, PRO792, PRO812, PRO865, PRO1075, PRO1126, PRO1130, PRO1154, PRO1244, PRO1246, PRO1274, PRO1286, PRO1294, PRO1303, PRO1304, PRO1312, PRO1313, PRO1376, PRO1387, PRO1561 or PRO216 polypeptide, in admixture with a pharmaceutically acceptable carrier;
- (2) a container containing said composition; and
- (3) a label affixed to said container, or a package insert included in said container referring to the use of said composition in the treatment of a cardiovascular, endothelial, and angiogenic disorder.

8. The article of manufacture of Claim 7, wherein said agonist is an anti-PRO172, anti-PRO178, anti-PRO179, anti-PRO182, anti-PRO187, anti-PRO188, anti-PRO195, anti-PRO212, anti-PRO214, anti-PRO217, anti-PRO224, anti-PRO231, anti-PRO235, anti-PRO245, anti-PRO261, anti-PRO269, anti-PRO287, anti-PRO301, anti-PRO323, anti-PRO331, anti-PRO356, anti-PRO364, anti-PRO526, anti-PRO538, anti-PRO713, anti-PRO719, anti-PRO771, anti-PRO788, anti-PRO792, anti-PRO812, anti-PRO865, anti-PRO1075, anti-PRO1126, anti-PRO1130, anti-PRO1154, anti-PRO1244, anti-PRO1246, anti-PRO1274, anti-PRO1286, anti-PRO1294, anti-PRO1303, anti-PRO1304, anti-PRO1312, anti-PRO1313, anti-PRO1376, anti-PRO1387, anti-PRO1561 or anti-PRO216 antibody.

9. The article of manufacture of Claim 7, wherein said antagonist is an anti-PRO172, anti-PRO178, anti-PRO179, anti-PRO182, anti-PRO187, anti-PRO188, anti-PRO195, anti-PRO212, anti-PRO214, anti-PRO217, anti-PRO224, anti-PRO231, anti-PRO235, anti-PRO245, anti-PRO261, anti-PRO269, anti-PRO287, anti-PRO301, anti-PRO323, anti-PRO331, anti-PRO356, anti-PRO364, anti-PRO526, anti-PRO538, anti-PRO713, anti-PRO719, anti-PRO771, anti-PRO788, anti-PRO792, anti-PRO812, anti-PRO865, anti-PRO1075, anti-PRO1126, anti-PRO1130, anti-PRO1154, anti-PRO1244, anti-PRO1246, anti-PRO1274, anti-PRO1286, anti-PRO1294, anti-PRO1303, anti-PRO1304, anti-PRO1312, anti-PRO1313, anti-PRO1376, anti-PRO1387, anti-PRO1561 or anti-PRO216 antibody.

10. The article of manufacture of Claim 7, wherein said composition comprises a therapeutically effective amount of said polypeptide or agonist or antagonist thereof, in admixture with said pharmaceutically acceptable carrier.

11. A method for identifying an agonist of a PRO172, PRO178, PRO179, PRO182, PRO187, PRO188, PRO195, PRO212, PRO214, PRO217, PRO224, PRO231, PRO235, PRO245, PRO261, PRO269, PRO287, PRO301, PRO323, PRO331, PRO356, PRO364, PRO526, PRO538, PRO713, PRO719, PRO771, PRO788, PRO792, PRO812, PRO865, PRO1075, PRO1126, PRO1130, PRO1154, PRO1244, PRO1246, PRO1274, PRO1286, PRO1294, PRO1303, PRO1304, PRO1312, PRO1313, PRO1376, PRO1387, PRO1561 or PRO216 polypeptide comprising:

(a) contacting cells and a test compound to be screened under conditions suitable for the induction of a cellular response normally induced by a PRO172, PRO178, PRO179, PRO182, PRO187, PRO188, PRO195, PRO212, PRO214, PRO217, PRO224, PRO231, PRO235, PRO245, PRO261, PRO269, PRO287, PRO301, PRO323, PRO331, PRO356, PRO364, PRO526, PRO538, PRO713, PRO719, PRO771, PRO788, PRO792, PRO812, PRO865, PRO1075, PRO1126, PRO1130, PRO1154, PRO1244, PRO1246, PRO1274, PRO1286, PRO1294, PRO1303, PRO1304, PRO1312, PRO1313, PRO1376, PRO1387, PRO1561 or PRO216 polypeptide; and

(b) determining the induction of said cellular response to determine if the test compound is an effective agonist, wherein the induction of said cellular response is indicative of said test compound being an effective agonist.

12. The method of Claim 11, wherein the cellular response normally induced by said PRO172, PRO178, PRO179, PRO182, PRO187, PRO188, PRO195, PRO212, PRO214, PRO217, PRO224, PRO231, PRO235, PRO245, PRO261, PRO269, PRO287, PRO301, PRO323, PRO331, PRO356, PRO364, PRO526, PRO538, PRO713, PRO719, PRO771, PRO788, PRO792, PRO812, PRO865, PRO1075, PRO1126, PRO1130, PRO1154, PRO1244, PRO1246, PRO1274, PRO1286, PRO1294, PRO1303, PRO1304, PRO1312, PRO1313, PRO1376, PRO1387, PRO1561 or PRO216 polypeptide is stimulation of cell proliferation.

13. A method for identifying a compound that inhibits an activity of a PRO172, PRO178, PRO179, PRO182, PRO187, PRO188, PRO195, PRO212, PRO214, PRO217, PRO224, PRO231, PRO235, PRO245, PRO261, PRO269, PRO287, PRO301, PRO323, PRO331, PRO356, PRO364, PRO526, PRO538, PRO713, PRO719, PRO771, PRO788, PRO792, PRO812, PRO865, PRO1075, PRO1126, PRO1130, PRO1154, PRO1244, PRO1246, PRO1274, PRO1286, PRO1294, PRO1303, PRO1304, PRO1312, PRO1313, PRO1376, PRO1387, PRO1561 or PRO216 polypeptide comprising contacting a test compound with said polypeptide under conditions and for a time sufficient to allow the test compound and polypeptide to interact and determining whether the activity of said polypeptide is inhibited.

14. A method for identifying a compound that inhibits an activity of a PRO172, PRO178, PRO179, PRO182, PRO187, PRO188, PRO195, PRO212, PRO214, PRO217, PRO224, PRO231, PRO235, PRO245, PRO261, PRO269, PRO287, PRO301, PRO323, PRO331, PRO356, PRO364, PRO526, PRO538, PRO713, PRO719, PRO771, PRO788, PRO792, PRO812, PRO865, PRO1075, PRO1126, PRO1130, PRO1154, PRO1244, PRO1246, PRO1274, PRO1286, PRO1294, PRO1303, PRO1304, PRO1312, PRO1313, PRO1376, PRO1387, PRO1561 or PRO216 polypeptide comprising the steps of:

- (a) contacting cells and a test compound to be screened in the presence of said polypeptide under conditions suitable for the induction of a cellular response normally induced by said polypeptide; and
- (b) determining the induction of said cellular response to determine if the test compound is an effective antagonist.

15. The method of Claim 14, wherein the cellular response normally induced by said polypeptide is stimulation of cell proliferation.

16. A method for identifying a compound that inhibits the expression of a PRO172, PRO178, PRO179, PRO182, PRO187, PRO188, PRO195, PRO212, PRO214, PRO217, PRO224, PRO231, PRO235, PRO245, PRO261, PRO269, PRO287, PRO301, PRO323, PRO331, PRO356, PRO364, PRO526, PRO538, PRO713, PRO719, PRO771, PRO788, PRO792, PRO812, PRO865, PRO1075, PRO1126, PRO1130, PRO1154, PRO1244, PRO1246, PRO1274, PRO1286, PRO1294, PRO1303, PRO1304, PRO1312, PRO1313, PRO1376, PRO1387, PRO1561 or PRO216 polypeptide in cells that normally express the polypeptide, wherein the method comprises contacting the cells with a test compound under conditions suitable for allowing expression of said polypeptide and determining whether the expression of said polypeptide is inhibited.

17. An agonist of a PRO172, PRO178, PRO179, PRO182, PRO187, PRO188, PRO195, PRO212, PRO214, PRO217, PRO224, PRO231, PRO235, PRO245, PRO261, PRO269, PRO287, PRO301, PRO323, PRO331, PRO356, PRO364, PRO526, PRO538, PRO713, PRO719, PRO771, PRO788, PRO792, PRO812, PRO865, PRO1075, PRO1126, PRO1130, PRO1154, PRO1244, PRO1246, PRO1274, PRO1286, PRO1294, PRO1303, PRO1304, PRO1312, PRO1313, PRO1376, PRO1387, PRO1561 or PRO216 polypeptide.

18. An antagonist of a PRO172, PRO178, PRO179, PRO182, PRO187, PRO188, PRO195, PRO212, PRO214, PRO217, PRO224, PRO231, PRO235, PRO245, PRO261, PRO269, PRO287, PRO301, PRO323, PRO331, PRO356, PRO364, PRO526, PRO538, PRO713, PRO719, PRO771, PRO788, PRO792, PRO812, PRO865, PRO1075, PRO1126, PRO1130, PRO1154, PRO1244, PRO1246, PRO1274, PRO1286, PRO1294, PRO1303, PRO1304, PRO1312, PRO1313, PRO1376, PRO1387, PRO1561 or PRO216 polypeptide.

19. A compound that inhibits the expression of a PRO172, PRO178, PRO179, PRO182, PRO187, PRO188, PRO195, PRO212, PRO214, PRO217, PRO224, PRO231, PRO235, PRO245, PRO261, PRO269, PRO287,

PRO301, PRO323, PRO331, PRO356, PRO364, PRO526, PRO538, PRO713, PRO719, PRO771, PRO788, PRO792, PRO812, PRO865, PRO1075, PRO1126, PRO1130, PRO1154, PRO1244, PRO1246, PRO1274, PRO1286, PRO1294, PRO1303, PRO1304, PRO1312, PRO1313, PRO1376, PRO1387, PRO1561 or PRO216 polypeptide in a mammalian cell which expresses said polypeptide.

20. The compound of Claim 19, wherein said compound is an antisense oligonucleotide.

21. An isolated antibody that binds to a PRO172, PRO178, PRO179, PRO182, PRO187, PRO188, PRO195, PRO212, PRO214, PRO217, PRO224, PRO231, PRO235, PRO245, PRO261, PRO269, PRO287, PRO301, PRO323, PRO331, PRO356, PRO364, PRO526, PRO538, PRO713, PRO719, PRO771, PRO788, PRO792, PRO812, PRO865, PRO1075, PRO1126, PRO1130, PRO1154, PRO1244, PRO1246, PRO1274, PRO1286, PRO1294, PRO1303, PRO1304, PRO1312, PRO1313, PRO1376, PRO1387, PRO1561 or PRO216 polypeptide.

22. The antibody of Claim 21 which is a monoclonal antibody.

23. The antibody of Claim 21 which is an antibody fragment.

24. The antibody of Claim 21 which is a single-chain antibody.

25. A method for diagnosing a disease or susceptibility to a disease which is related to a mutation in a PRO172, PRO178, PRO179, PRO182, PRO187, PRO188, PRO195, PRO212, PRO214, PRO217, PRO224, PRO231, PRO235, PRO245, PRO261, PRO269, PRO287, PRO301, PRO323, PRO331, PRO356, PRO364, PRO526, PRO538, PRO713, PRO719, PRO771, PRO788, PRO792, PRO812, PRO865, PRO1075, PRO1126, PRO1130, PRO1154, PRO1244, PRO1246, PRO1274, PRO1286, PRO1294, PRO1303, PRO1304, PRO1312, PRO1313, PRO1376, PRO1387, PRO1561 or PRO216 polypeptide-encoding nucleic acid sequence comprising determining the presence or absence of said mutation in said polypeptide-encoding nucleic acid sequence, wherein the presence or absence of said mutation is indicative of the presence of said disease or susceptibility to said disease.

26. A method of diagnosing a cardiovascular, endothelial or angiogenic disorder in a mammal which comprises analyzing the level of expression of a gene encoding a PRO172, PRO178, PRO179, PRO182, PRO187, PRO188, PRO195, PRO212, PRO214, PRO217, PRO224, PRO231, PRO235, PRO245, PRO261, PRO269, PRO287, PRO301, PRO323, PRO331, PRO356, PRO364, PRO526, PRO538, PRO713, PRO719, PRO771, PRO788, PRO792, PRO812, PRO865, PRO1075, PRO1126, PRO1130, PRO1154, PRO1244, PRO1246, PRO1274, PRO1286, PRO1294, PRO1303, PRO1304, PRO1312, PRO1313, PRO1376, PRO1387, PRO1561 or PRO216 polypeptide (a) in a test sample of tissue cells obtained from said mammal, and (b) in a control sample

of known normal tissue cells of the same cell type, wherein a higher or lower expression level in the test sample as compared to the control sample is indicative of the presence of a cardiovascular, endothelial or angiogenic disorder in said mammal.

27. A method of diagnosing a cardiovascular, endothelial or angiogenic disorder in a mammal which comprises detecting the presence or absence of a PRO172, PRO178, PRO179, PRO182, PRO187, PRO188, PRO195, PRO212, PRO214, PRO217, PRO224, PRO231, PRO235, PRO245, PRO261, PRO269, PRO287, PRO301, PRO323, PRO331, PRO356, PRO364, PRO526, PRO538, PRO713, PRO719, PRO771, PRO788, PRO792, PRO812, PRO865, PRO1075, PRO1126, PRO1130, PRO1154, PRO1244, PRO1246, PRO1274, PRO1286, PRO1294, PRO1303, PRO1304, PRO1312, PRO1313, PRO1376, PRO1387, PRO1561 or PRO216 polypeptide in a test sample of tissue cells obtained from said mammal, wherein the presence or absence of said polypeptide in said test sample is indicative of the presence of a cardiovascular, endothelial or angiogenic disorder in said mammal.

28. A method of diagnosing a cardiovascular, endothelial or angiogenic disorder in a mammal comprising (a) contacting an anti-PRO172, anti-PRO178, anti-PRO179, anti-PRO182, anti-PRO187, anti-PRO188, anti-PRO195, anti-PRO212, anti-PRO214, anti-PRO217, anti-PRO224, anti-PRO231, anti-PRO235, anti-PRO245, anti-PRO261, anti-PRO269, anti-PRO287, anti-PRO301, anti-PRO323, anti-PRO331, anti-PRO356, anti-PRO364, anti-PRO526, anti-PRO538, anti-PRO713, anti-PRO719, anti-PRO771, anti-PRO788, anti-PRO792, anti-PRO812, anti-PRO865, anti-PRO1075, anti-PRO1126, anti-PRO1130, anti-PRO1154, anti-PRO1244, anti-PRO1246, anti-PRO1274, anti-PRO1286, anti-PRO1294, anti-PRO1303, anti-PRO1304, anti-PRO1312, anti-PRO1313, anti-PRO1376, anti-PRO1387, anti-PRO1561 or anti-PRO216 antibody with a test sample of tissue cells obtained from the mammal, and (b) detecting the formation of a complex between said antibody and a PRO172, PRO178, PRO179, PRO182, PRO187, PRO188, PRO195, PRO212, PRO214, PRO217, PRO224, PRO231, PRO235, PRO245, PRO261, PRO269, PRO287, PRO301, PRO323, PRO331, PRO356, PRO364, PRO526, PRO538, PRO713, PRO719, PRO771, PRO788, PRO792, PRO812, PRO865, PRO1075, PRO1126, PRO1130, PRO1154, PRO1244, PRO1246, PRO1274, PRO1286, PRO1294, PRO1303, PRO1304, PRO1312, PRO1313, PRO1376, PRO1387, PRO1561 or PRO216 polypeptide in the test sample, wherein the formation of said complex is indicative of the presence of a cardiovascular, endothelial or angiogenic disorder in the mammal.

29. A method for determining the presence of a PRO172, PRO178, PRO179, PRO182, PRO187, PRO188, PRO195, PRO212, PRO214, PRO217, PRO224, PRO231, PRO235, PRO245, PRO261, PRO269, PRO287, PRO301, PRO323, PRO331, PRO356, PRO364, PRO526, PRO538, PRO713, PRO719, PRO771, PRO788, PRO792, PRO812, PRO865, PRO1075, PRO1126, PRO1130, PRO1154, PRO1244, PRO1246, PRO1274, PRO1286, PRO1294, PRO1303, PRO1304, PRO1312, PRO1313, PRO1376, PRO1387, PRO1561 or PRO216 polypeptide in a sample comprising contacting a sample suspected of containing said polypeptide with an anti-PRO172, anti-PRO178, anti-PRO179, anti-PRO182, anti-PRO187, anti-PRO188, anti-PRO195, anti-PRO212, anti-

PRO214, anti-PRO217, anti-PRO224, anti-PRO231, anti-PRO235, anti-PRO245, anti-PRO261, anti-PRO269, anti-PRO287, anti-PRO301, anti-PRO323, anti-PRO331, anti-PRO356, anti-PRO364, anti-PRO526, anti-PRO538, anti-PRO713, anti-PRO719, anti-PRO771, anti-PRO788, anti-PRO792, anti-PRO812, anti-PRO865, anti-PRO1075, anti-PRO1126, anti-PRO1130, anti-PRO1154, anti-PRO1244, anti-PRO1246, anti-PRO1274, anti-PRO1286, anti-PRO1294, anti-PRO1303, anti-PRO1304, anti-PRO1312, anti-PRO1313, anti-PRO1376, anti-PRO1387, anti-PRO1561 or anti-PRO216 antibody and determining binding of said antibody to a component of said sample.

30. A cardiovascular, endothelial or angiogenic disorder diagnostic kit comprising an anti-PRO172, anti-PRO178, anti-PRO179, anti-PRO182, anti-PRO187, anti-PRO188, anti-PRO195, anti-PRO212, anti-PRO214, anti-PRO217, anti-PRO224, anti-PRO231, anti-PRO235, anti-PRO245, anti-PRO261, anti-PRO269, anti-PRO287, anti-PRO301, anti-PRO323, anti-PRO331, anti-PRO356, anti-PRO364, anti-PRO526, anti-PRO538, anti-PRO713, anti-PRO719, anti-PRO771, anti-PRO788, anti-PRO792, anti-PRO812, anti-PRO865, anti-PRO1075, anti-PRO1126, anti-PRO1130, anti-PRO1154, anti-PRO1244, anti-PRO1246, anti-PRO1274, anti-PRO1286, anti-PRO1294, anti-PRO1303, anti-PRO1304, anti-PRO1312, anti-PRO1313, anti-PRO1376, anti-PRO1387, anti-PRO1561 or anti-PRO216 antibody and a carrier in suitable packaging.

31. A method for treating a cardiovascular, endothelial or angiogenic disorder in a mammal comprising administering to the mammal a therapeutically effective amount of a PRO172, PRO178, PRO179, PRO182, PRO187, PRO188, PRO195, PRO212, PRO214, PRO217, PRO224, PRO231, PRO235, PRO245, PRO261, PRO269, PRO287, PRO301, PRO323, PRO331, PRO356, PRO364, PRO526, PRO538, PRO713, PRO719, PRO771, PRO788, PRO792, PRO812, PRO865, PRO1075, PRO1126, PRO1130, PRO1154, PRO1244, PRO1246, PRO1274, PRO1286, PRO1294, PRO1303, PRO1304, PRO1312, PRO1313, PRO1376, PRO1387, PRO1561 or PRO216 polypeptide or an agonist or antagonist thereof.

32. The method according to Claim 31, wherein the mammal is human.

33. The method of Claim 32, wherein the human has suffered myocardial infarction.

34. The method of Claim 32, wherein the human has cardiac hypertrophy, trauma, a cancer, or age-related macular degeneration.

35. The method of Claim 34, wherein the cardiac hypertrophy is characterized by the presence of an elevated level of $\text{PGF}_{2\alpha}$.

36. The method of Claim 31, wherein the PRO172, PRO178, PRO179, PRO182, PRO187, PRO188, PRO195, PRO212, PRO214, PRO217, PRO224, PRO231, PRO235, PRO245, PRO261, PRO269, PRO287, PRO301, PRO323, PRO331, PRO356, PRO364, PRO526, PRO538, PRO713, PRO719, PRO771, PRO788,

PRO792, PRO812, PRO865, PRO1075, PRO1126, PRO1130, PRO1154, PRO1244, PRO1246, PRO1274, PRO1286, PRO1294, PRO1303, PRO1304, PRO1312, PRO1313, PRO1376, PRO1387, PRO1561 or PRO216 polypeptide is administered together with a cardiovascular, endothelial or angiogenic agent.

37. The method of Claim 34, wherein the PRO172, PRO178, PRO179, PRO182, PRO187, PRO188, PRO195, PRO212, PRO214, PRO217, PRO224, PRO231, PRO235, PRO245, PRO261, PRO269, PRO287, PRO301, PRO323, PRO331, PRO356, PRO364, PRO526, PRO538, PRO713, PRO719, PRO771, PRO788, PRO792, PRO812, PRO865, PRO1075, PRO1126, PRO1130, PRO1154, PRO1244, PRO1246, PRO1274, PRO1286, PRO1294, PRO1303, PRO1304, PRO1312, PRO1313, PRO1376, PRO1387, PRO1561 or PRO216 polypeptide is administered following primary angioplasty.

38. The method of Claim 31, wherein the cardiovascular, endothelial or angiogenic disorder is cancer.

39. The method of Claim 38, wherein the PRO172, PRO178, PRO179, PRO182, PRO187, PRO188, PRO195, PRO212, PRO214, PRO217, PRO224, PRO231, PRO235, PRO245, PRO261, PRO269, PRO287, PRO301, PRO323, PRO331, PRO356, PRO364, PRO526, PRO538, PRO713, PRO719, PRO771, PRO788, PRO792, PRO812, PRO865, PRO1075, PRO1126, PRO1130, PRO1154, PRO1244, PRO1246, PRO1274, PRO1286, PRO1294, PRO1303, PRO1304, PRO1312, PRO1313, PRO1376, PRO1387, PRO1561 or PRO216 polypeptide is administered in combination with a chemotherapeutic agent, a growth inhibitory agent or a cytotoxic agent.

40. The method of Claim 31 wherein said agonist is an anti-PRO172, anti-PRO178, anti-PRO179, anti-PRO182, anti-PRO187, anti-PRO188, anti-PRO195, anti-PRO212, anti-PRO214, anti-PRO217, anti-PRO224, anti-PRO231, anti-PRO235, anti-PRO245, anti-PRO261, anti-PRO269, anti-PRO287, anti-PRO301, anti-PRO323, anti-PRO331, anti-PRO356, anti-PRO364, anti-PRO526, anti-PRO538, anti-PRO713, anti-PRO719, anti-PRO771, anti-PRO788, anti-PRO792, anti-PRO812, anti-PRO865, anti-PRO1075, anti-PRO1126, anti-PRO1130, anti-PRO1154, anti-PRO1244, anti-PRO1246, anti-PRO1274, anti-PRO1286, anti-PRO1294, anti-PRO1303, anti-PRO1304, anti-PRO1312, anti-PRO1313, anti-PRO1376, anti-PRO1387, anti-PRO1561 or anti-PRO216 antibody.

41. The method of Claim 31 wherein said antagonist is an anti-PRO172, anti-PRO178, anti-PRO179, anti-PRO182, anti-PRO187, anti-PRO188, anti-PRO195, anti-PRO212, anti-PRO214, anti-PRO217, anti-PRO224, anti-PRO231, anti-PRO235, anti-PRO245, anti-PRO261, anti-PRO269, anti-PRO287, anti-PRO301, anti-PRO323, anti-PRO331, anti-PRO356, anti-PRO364, anti-PRO526, anti-PRO538, anti-PRO713, anti-PRO719, anti-PRO771, anti-PRO788, anti-PRO792, anti-PRO812, anti-PRO865, anti-PRO1075, anti-PRO1126, anti-PRO1130, anti-PRO1154, anti-PRO1244, anti-PRO1246, anti-PRO1274, anti-PRO1286, anti-PRO1294, anti-PRO1303, anti-PRO1304, anti-PRO1312, anti-PRO1313, anti-PRO1376, anti-PRO1387, anti-PRO1561 or anti-PRO216 antibody.

42. A method for treating a cardiovascular, endothelial or angiogenic disorder in a mammal comprising administering to the mammal a nucleic acid molecule that encodes a PRO172, PRO178, PRO179, PRO182, PRO187, PRO188, PRO195, PRO212, PRO214, PRO217, PRO224, PRO231, PRO235, PRO245, PRO261, PRO269, PRO287, PRO301, PRO323, PRO331, PRO356, PRO364, PRO526, PRO538, PRO713, PRO719, PRO771, PRO788, PRO792, PRO812, PRO865, PRO1075, PRO1126, PRO1130, PRO1154, PRO1244, PRO1246, PRO1274, PRO1286, PRO1294, PRO1303, PRO1304, PRO1312, PRO1313, PRO1376, PRO1387, PRO1561 or PRO216 polypeptide or agonist or antagonist thereof

43. The method of Claim 42 wherein said agonist is an anti-PRO172, anti-PRO178, anti-PRO179, anti-PRO182, anti-PRO187, anti-PRO188, anti-PRO195, anti-PRO212, anti-PRO214, anti-PRO217, anti-PRO224, anti-PRO231, anti-PRO235, anti-PRO245, anti-PRO261, anti-PRO269, anti-PRO287, anti-PRO301, anti-PRO323, anti-PRO331, anti-PRO356, anti-PRO364, anti-PRO526, anti-PRO538, anti-PRO713, anti-PRO719, anti-PRO771, anti-PRO788, anti-PRO792, anti-PRO812, anti-PRO865, anti-PRO1075, anti-PRO1126, anti-PRO1130, anti-PRO1154, anti-PRO1244, anti-PRO1246, anti-PRO1274, anti-PRO1286, anti-PRO1294, anti-PRO1303, anti-PRO1304, anti-PRO1312, anti-PRO1313, anti-PRO1376, anti-PRO1387, anti-PRO1561 or anti-PRO216 antibody.

44. The method of Claim 42 wherein said antagonist is an anti-PRO172, anti-PRO178, anti-PRO179, anti-PRO182, anti-PRO187, anti-PRO188, anti-PRO195, anti-PRO212, anti-PRO214, anti-PRO217, anti-PRO224, anti-PRO231, anti-PRO235, anti-PRO245, anti-PRO261, anti-PRO269, anti-PRO287, anti-PRO301, anti-PRO323, anti-PRO331, anti-PRO356, anti-PRO364, anti-PRO526, anti-PRO538, anti-PRO713, anti-PRO719, anti-PRO771, anti-PRO788, anti-PRO792, anti-PRO812, anti-PRO865, anti-PRO1075, anti-PRO1126, anti-PRO1130, anti-PRO1154, anti-PRO1244, anti-PRO1246, anti-PRO1274, anti-PRO1286, anti-PRO1294, anti-PRO1303, anti-PRO1304, anti-PRO1312, anti-PRO1313, anti-PRO1376, anti-PRO1387, anti-PRO1561 or anti-PRO216 antibody.

45. The method of Claim 42, wherein the mammal is human.

46. The method of Claim 42, wherein the nucleic acid molecule is administered via *ex vivo* gene therapy.

47. A recombinant retroviral particle comprising a retroviral vector consisting essentially of (1) a promoter, (2) nucleic acid encoding a PRO172, PRO178, PRO179, PRO182, PRO187, PRO188, PRO195, PRO212, PRO214, PRO217, PRO224, PRO231, PRO235, PRO245, PRO261, PRO269, PRO287, PRO301, PRO323, PRO331, PRO356, PRO364, PRO526, PRO538, PRO713, PRO719, PRO771, PRO788, PRO792, PRO812, PRO865, PRO1075, PRO1126, PRO1130, PRO1154, PRO1244, PRO1246, PRO1274, PRO1286, PRO1294, PRO1303, PRO1304, PRO1312, PRO1313, PRO1376, PRO1387, PRO1561 or PRO216 polypeptide or agonist or antagonist thereof, and (3) a signal sequence for cellular secretion of the polypeptide, wherein the retroviral vector is in association with retroviral structural proteins.

48. An *ex vivo* producer cell comprising a nucleic acid construct that expresses retroviral structural proteins and also comprises a retroviral vector consisting essentially of (1) a promoter, (2) nucleic acid encoding a PRO172, PRO178, PRO179, PRO182, PRO187, PRO188, PRO195, PRO212, PRO214, PRO217, PRO224, PRO231, PRO235, PRO245, PRO261, PRO269, PRO287, PRO301, PRO323, PRO331, PRO356, PRO364, PRO526, PRO538, PRO713, PRO719, PRO771, PRO788, PRO792, PRO812, PRO865, PRO1075, PRO1126, PRO1130, PRO1154, PRO1244, PRO1246, PRO1274, PRO1286, PRO1294, PRO1303, PRO1304, PRO1312, PRO1313, PRO1376, PRO1387, PRO1561 or PRO216 polypeptide or agonist or antagonist thereof, and (3) a signal sequence for cellular secretion of the polypeptide, wherein said producer cell packages the retroviral vector in association with the structural proteins to produce recombinant retroviral particles.

49. A method for inhibiting endothelial cell growth in a mammal comprising administering to the mammal (a) a PRO172, PRO178, PRO179, PRO187, PRO188, PRO214, PRO216, PRO217, PRO235, PRO261, PRO287, PRO301, PRO323, PRO331, PRO364, PRO538, PRO713, PRO719, PRO788, PRO812, PRO865, PRO1126, PRO1130, PRO1246, PRO1274, PRO1294, PRO1304, PRO1376 or PRO1387 polypeptide or agonist thereof, wherein endothelial cell growth in said mammal is inhibited.

50. A method for stimulating endothelial cell growth in a mammal comprising administering to the mammal a PRO179, PRO212, PRO245, PRO771, PRO1075, PRO1154, PRO1244, PRO1286, PRO1303, PRO1313, PRO1376 or PRO1561 polypeptide or agonist thereof, wherein endothelial cell growth in said mammal is stimulated.

51. A method for inhibiting endothelial cell growth in a mammal comprising administering to the mammal an antagonist of a PRO179, PRO212, PRO245, PRO771, PRO1075, PRO1154, PRO1244, PRO1286, PRO1303, PRO1313, PRO1376 or PRO1561 polypeptide, wherein endothelial cell growth in said mammal is inhibited.

52. A method for stimulating endothelial cell growth in a mammal comprising administering to the mammal an antagonist of a PRO172, PRO178, PRO179, PRO187, PRO188, PRO214, PRO216, PRO217, PRO235, PRO261, PRO287, PRO301, PRO323, PRO331, PRO364, PRO538, PRO713, PRO719, PRO788, PRO812, PRO865, PRO1126, PRO1130, PRO1246, PRO1274, PRO1294, PRO1304, PRO1376 or PRO1387 polypeptide, wherein endothelial cell growth in said mammal is stimulated.

53. A method for reducing cardiac hypertrophy in a mammal comprising administering to the mammal a PRO269 or PRO356 polypeptide or agonist thereof, wherein cardiac hypertrophy in said mammal is reduced.

54. The method of Claim 53, wherein the cardiac hypertrophy has been induced by myocardial infarction.

55. A method for inducing cardiac hypertrophy in a mammal comprising administering to the mammal a

PRO179, PRO182, PRO195, PRO224, PRO231, PRO526, PRO713, PRO792, PRO1246 or PRO1312 polypeptide or agonist thereof, wherein said cardiac hypertrophy in said mammal is induced.

56. A method for reducing cardiac hypertrophy in a mammal comprising administering to the mammal an antagonist of a PRO179, PRO182, PRO195, PRO224, PRO231, PRO526, PRO713, PRO792, PRO1246 or PRO1312 polypeptide, wherein cardiac hypertrophy in said mammal is reduced.

57. A method for inducing cardiac hypertrophy in a mammal comprising administering to the mammal an antagonist of a PRO269 or PRO356 polypeptide, wherein cardiac hypertrophy in said mammal is induced.

58. A method for inhibiting angiogenesis induced by a PRO179, PRO212, PRO245, PRO771, PRO1075, PRO1154, PRO1244, PRO1286, PRO1303, PRO1313, PRO1376 or PRO1561 polypeptide in a mammal comprising administering a therapeutically effective amount of an anti-PRO179, anti-PRO212, anti-PRO245, anti-PRO771, anti-PRO1075, anti-PRO1154, anti-PRO1244, anti-PRO1286, anti-PRO1303, anti-PRO1313, anti-PRO1376 or anti-PRO1561 antibody to the mammal, wherein said angiogenesis is inhibited.

59. A method for stimulating angiogenesis induced by a PRO179, PRO212, PRO245, PRO771, PRO1075, PRO1154, PRO1244, PRO1286, PRO1303, PRO1313, PRO1376 or PRO1561 polypeptide in a mammal comprising administering a therapeutically effective amount of said polypeptide to the mammal, whereby said angiogenesis is stimulated.

60. Isolated nucleic acid having at least 80% nucleic acid sequence identity to a nucleotide sequence that encodes an amino acid sequence selected from the group consisting of the amino acid sequence shown in Figure 2 (SEQ ID NO:4), Figure 4 (SEQ ID NO:9), Figure 6 (SEQ ID NO:14), Figure 8 (SEQ ID NO:16), Figure 10 (SEQ ID NO:21), Figure 12 (SEQ ID NO:26), Figure 14 (SEQ ID NO:31), Figure 16 (SEQ ID NO:36), Figure 18 (SEQ ID NO:41), Figure 20 (SEQ ID NO:46), Figure 22 (SEQ ID NO:51), Figure 24 (SEQ ID NO:56), Figure 26 (SEQ ID NO:62), Figure 28 (SEQ ID NO:67), Figure 30 (SEQ ID NO:72), Figure 32 (SEQ ID NO:77), Figure 34 (SEQ ID NO:85), Figure 36 (SEQ ID NO:90), Figure 38 (SEQ ID NO:98), Figure 40 (SEQ ID NO:107), Figure 42 (SEQ ID NO:112), Figure 44 (SEQ ID NO:117), Figure 46 (SEQ ID NO:127), Figure 48 (SEQ ID NO:132), Figure 50 (SEQ ID NO:137), Figure 52 (SEQ ID NO:143), Figure 54 (SEQ ID NO:148), Figure 56 (SEQ ID NO:153), Figure 58 (SEQ ID NO:155), Figure 60 (SEQ ID NO:160), Figure 62 (SEQ ID NO:162), Figure 64 (SEQ ID NO:170), Figure 66 (SEQ ID NO:181), Figure 68 (SEQ ID NO:183), Figure 70 (SEQ ID NO:191), Figure 72 (SEQ ID NO:193), Figure 74 (SEQ ID NO:195), Figure 76 (SEQ ID NO:197), Figure 78 (SEQ ID NO:199), Figure 80 (SEQ ID NO:201), Figure 82 (SEQ ID NO:203), Figure 84 (SEQ ID NO:205), Figure 86 (SEQ ID NO:214), Figure 88 (SEQ ID NO:216), Figure 90 (SEQ ID NO:218), Figure 92 (SEQ ID NO:220), Figure 94 (SEQ ID NO:222), and Figure 96 (SEQ ID NO:227).